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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/766,682	01/27/2004	John C. Reed	066821-0267	2878

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EXAMINER	
WOOLWINE, SAMUEL C	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 07/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/766,682	REED ET AL.	
	Examiner	Art Unit	
	Samuel Woolwine	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *9-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/8/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicants' election with traverse of Group I, claims 1-8, in the response filed 5/26/2006 is acknowledged. Claims 9-22 are withdrawn from further consideration. Applicants have traversed with respect to the division of Group I claims from Group III. Applicants concede that the two groups are patentably distinct, but argues that a search of both groups would not constitute an undue burden. Applicants contend that a search for each group will "likely" reveal art relevant to the other group. This argument has been carefully considered but is not persuasive. While individual searches for both groups would be partially overlapping, the searches would not necessarily be co-extensive because, as pointed out in the previous Office Action, the nucleic acids of Group I could be used in a materially different method than the methods of Group III. Even if anticipatory art is found against the claims of Group I, additional search may be required for Group III since the latter group includes additional limitations over and above those found in Group I. Therefore, the searches for each of Groups I and III would be different and burdensome. Since Applicants have elected the product claims, if the product claims are found allowable, method claims that depend from or otherwise include all the limitations of the allowed product claims will be rejoined as a matter of right. Therefore the requirement for restriction is made FINAL.

Priority

Claims 1-8 are directed to isolated nucleic molecules encoding a CARD3X-2 polypeptide (representing a newly identified splice variant of the CARD3X gene, see

abstract) comprising the amino acid sequence as set forth in SEQ ID NO: 197 or a domain thereof selected from a CARD domain, NACHT domain or LRR domain. A search of the parent application, 09/864,921, does not find the term "CARD3X-2". A search for SEQ ID NOS: 196 and 197 of the instant application finds these sequences absent in the parent application. Likewise, provisional applications 60/367,337 and 60/275,980 only contain 109 and 166 sequences, respectively, and the term "CARD3X-2" was not found in a review of these documents. Therefore, claims 1-8 of the instant application will only be afforded priority to the filing date 01/27/2004.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-8 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. The current claims are drawn to isolated nucleic molecules encoding a CARD3X-2 polypeptide (representing a newly identified splice variant of the CARD3X gene, see abstract) comprising the amino acid sequence as set forth in SEQ ID NO: 197 or a domain thereof selected from a CARD domain, NACHT domain or LRR domain.

Credible Utility

Following the requirements of the Utility Guidelines (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for Utility.), the first inquiry is whether a credible utility is cited in the specification for use of the nucleic acid

molecule which encodes SEQ ID NO: 197. The following cited utilities for the claimed nucleic acid molecules were found in an examination of the specification:

1. used to produce the CARD3X-2 polypeptide (para [0011], [0084])
2. used to identify nucleic acid encoding CARD3X-2 polypeptide (para [0013], [0084])
3. reach through utility for the CARD3X-2 polypeptide (as a CARD-containing polypeptide) to "alter biochemical processes such as apoptosis, NF-kB induction, cytokine processing, cytokine receptor signaling, caspase-mediated proteolysis, thus having modulating effects on cell life and death, inflammation, cell adhesion, and other cellular and biochemical processes" (para [0037])
4. reach through utility for the CARD3X-2 polypeptide (as a CARD-containing polypeptide) to "identify CARD-binding agents and CARD-associated polypeptides" (para [0038])
5. reach through utility for the CARD3X-2 polypeptide (specifically) as a new drug target or diagnostic marker (para [0042])

Regarding credible utility, items 1, 2 and 4 above would certainly be regarded as credible. Item 3 would also be credible in that the CARD3X-2 polypeptide would be expected to modulate at least some cellular process, as would any protein. Item 5 is also credible, since in theory any polypeptide can be a drug target or (if associated with a disease) a diagnostic marker. It is noted, however, that Applicants have shown no association between CARD3X-2 and any disease.

Applicants have also demonstrated that expression of CARD3X in HEK2932T cells leads to induction of NF-kB (para [0353]) and that CARD3X associates with pro-caspase-1 (para [0356]). Likewise, Applicant demonstrates that expression of CARD3X together with pro-caspase-1 in HEK2932T cells results in significant IL-1β secretion (para [0357]). Whether the alternate form of the protein, i.e. CARD3X-2, performs these functions is simply unknown. Applicants comment (para [0041]) that "these and other splice variants can encode protein isoforms that have physiological activities that differ in degree or type from related isoforms", thus casting doubt on any assertion that CARD3X-2 possesses the same biological properties as CARD3X.

Upon identification of credible utilities, the next issue is whether there are any well established utilities for the nucleic acid molecule which encodes SEQ ID NO: 197, including 15-mer fragments of such nucleic acid molecules. No well established utilities for this nucleic acid molecule which encodes SEQ ID NO: 197 are identified in either the specification or in the cited prior art.

Substantial utility

Given the absence of a well established utility, the next issue is whether any credible utilities are substantial utilities. Here, there is no evidence of any substantial utility. No particular use for SEQ ID NO: 197 is found in the specification nor is there any use for any method involving SEQ ID NO: 197.

As noted in the utility guidelines, methods of treating unspecified diseases, basic research on a product to identify properties, intermediate products which themselves lack substantial utility are all insubstantial utilities (see page 6 of the Utility guideline

training materials). Items 1-5 above all fall into this category. If there were evidence of the association of SEQ ID NO: 197 with any disease state or with some other biological phenotype, this evidence might be considered regarding a substantial utility. However, no such evidence is found.

The cited utilities 1-5 above of CARD3X-2 nucleic acids and corresponding polypeptides have less "real world" significance than the amount of utility found insufficient by the Supreme court in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966). In *Brenner*, a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

The instant claims are drawn to polynucleotides encoding a protein (SEQ ID NO: 197) which has no identified cellular role, no particular cellular phenotype and is not associated with any disease. The function of the CARD3X-2 is as yet undetermined with no known function or biological significance. Until some actual and specific

significance can be attributed to the protein identified in the specification, or the gene encoding it, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there is no immediately apparent or "real world" utility as of the filing date directly consistent with *Brenner v. Manson*. Therefore, it is concluded that the claims lack substantial utility.

Specific Utility

In the current case, there is no specific utility for SEQ ID NO: 197 or methods using this sequence. No specific association of SEQ ID NO: 197 and any disease or even a specific biological phenotype is provided in the specification. The specification discusses a wide variety of phenotypes which might be influenced by CARD3X-2, SEQ ID NO: 197, such as cytokine processing, NF-kB activity or apoptosis (para [0037]), but does not specifically teach any use for the sequence in association with these multiple generic possibilities. Applicant asserts that CARD3X-2 is "likely expressed under physiological conditions in which activation of NF-kB is required" (para [0312]) but offers no evidence whatsoever to substantiate this assertion.

Claims 1-8 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility, a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to any nucleic acid encoding a CARD3X-2 polypeptide or a domain thereof selected from a CARD domain, NACHT domain, or LRR domain. The language of claim 1 can be interpreted to encompass not only the CARD, NACHT and LRR domains of the protein of SEQ ID NO:197 (which domains are not *explicitly* defined), but also generic CARD, NACHT and LRR domains found in other polypeptides. For example, Enkhbayar et al shows that LRR domains are found in over 2000 proteins (see first sentence of abstract), which number far surpasses what Applicant has disclosed. Similarly, CARD domains are found in a wide variety of proteins, as shown by the following definition:

> Caspase recruitment domains, or CARD domains, are interaction motifs found in a wide array of proteins, typcially those involved in processes relating to inflammation and apoptosis. These domains mediate the formation of larger protein complexes via direct interactions between individual CARDs. CARD domains are found on a strikingly wide range of proteins, including helicases, kinases, mitochondrial proteins, caspases, and other cytoplasmic factors. (http://en.wikipedia.org/wiki/CARD_domain, accessed 07/05/2006)

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the

written description inquiry, whatever is now claimed (See *Vas-Cath* at page 1117)." The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed (See *Vas-Cath* at page 1116)."

The skilled artisan cannot envision the detailed chemical structure of the encompassed nucleic acids. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993), and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. In *Fiddes v. Baird*, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1404, 1405 held that:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that 'the inventor invented the claimed invention.' *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (' [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.'). Thus, an applicant complies with the written description requirement 'by describing the invention, with all its claimed limitations, not that which makes it obvious,' and by using 'such descriptive means as words, structures, figures, diagrams, formulas,

etc., that set forth the claimed invention.' *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, 'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, 'an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself.' Id. at 1170, 25 USPQ2d at 1606."

Accordingly, absent a teaching of a representative number of polypeptides comprising each of the domains recited in claim 1, such that one of ordinary skill in the art could envision the entire, the specification provides insufficient written description to support the broadly claimed genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Nunez et al (US 20020197616 A1, publication of application 10/002,974).

With regard to claims 1-3, Nunez teaches a nucleic acid sequence (SEQ ID NO:53 of application 10/002,974; see figure 20 of Nunez) that is 100% identical to SEQ ID NO:196 of the instant application. SEQ ID NO:196 of the instant application is a nucleic acid sequence, the translation of which results in the amino acid sequence of SEQ ID NO:197. Additionally, Nunez teaches "an isolated and purified nucleic acid comprising a sequence encoding a protein selected from the group consisting of SEQ ID NOs: 2, 3, and 34" (para [0014]). SEQ ID NO:3 of Nunez is 100% identical to SEQ ID NO:197 of the instant application (see figure 14 of Nunez).

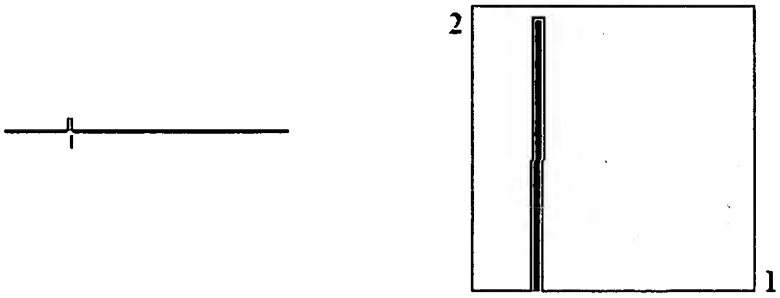
With regard to claim 4, the term "cDNA" imparts no structural limitation on the claimed nucleic acid molecule to distinguish it from SEQ ID NO:53 of Nunez.

With regard to claims 5 and 6, Nunez further teaches (para [0014]): "In some embodiments, the nucleic acid sequence is operably linked to a heterologous promoter. In some embodiments, the nucleic acid sequence is contained within a vector. In some further embodiments, the vector is within a host cell."

With regard to claims 7 and 8, Nunez teaches (para [0025]) an assay that "comprises a nucleic acid probe that hybridizes under stringent conditions to a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 70-83." Note that SEQ ID NOs: 70-83 of Nunez are all at least 15 nucleotides in length. In addition, at least SEQ ID NO: 70 of Nunez is found within SEQ ID NO:196 of the instant application:

Sequence 1: lcl|1_SEQID NO:196 (10/766682)
Length = 3042 (1 .. 3042)

Sequence 2: lcl|2_SEQID NO:70 (10/002974)
Length = 25 (1 .. 25)



NOTE:Bitscore and expect value are calculated based on the size of the nr database.

NOTE:If protein translation is reversed, please repeat the search with reverse strand of the query sequence.

```
 Score = 48.8 bits (25),  Expect = 0.11
 Identities = 25/25 (100%), Gaps = 0/25 (0%)
 Strand=Plus/Plus

Query  699  GGCAGATGTGGGCATGGCTGGACCC  723
            |||||||||||||||||||||||||
Sbjct  1    GGCAGATGTGGGCATGGCTGGACCC  25
```

Nunez further teaches (para [0153]): "It is contemplated that any probe used in the present invention will be labeled with any 'reporter molecule,' so that is detectable in any detection system, including, but not limited to enzyme (e.g., ELISA, as well as enzyme-based histochemical assays), fluorescent, radioactive, and luminescent systems."

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Woolwine whose telephone number is (571) 272-1144. The examiner can normally be reached on Mon-Fri 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

scw

JEFFREY FREDMAN
PRIMARY EXAMINER